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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,416	02/19/2002	Mechthild Rieping	218162US0X	2415
22850	7590	04/20/2004		EXAMINER
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			KERR, KATHLEEN M	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,416	RIEPING ET AL.	
	Examiner Kathleen M Kerr	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 26 January 2004.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-22 is/are pending in the application.
 - 4a) Of the above claim(s) 16-22 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-15 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 9/3/02.
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on November 25, 2003), Applicants filed an election received on January 26, 2004. Claims 1-22 are pending in the instant Office action.

Election

2. Applicant's election with traverse of Group I, Claims 1-15, in Paper No. received on January 26, 2004 is acknowledged. The traversal is on the ground(s) that no adequate reasons to support the finding of patentably distinctness were set forth by the Office in the restriction requirement. This is not found persuasive because reasoning as well as examples was previously described. Applicants also argue that no search burden exists for the Groups to be searched together. This is not found persuasive based on the clear search burden of different classifications for the different Groups cited in the restriction requirement.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-22 are pending. Claims 16-22 are withdrawn from consideration as non-elected invention. Claims 1-15 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the U.S. Provisional Application Nos. 60/283,612 and 60/248,210 filed on April 16, 2001 and November 15, 2000, respectively via the parent continuation application U.S. 09/987,541 filed on November 15,

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2001. This instant application is also granted the benefit of priority for foreign application DE 101 12 107.58 filed on March 14, 2001 as requested in the declaration. The Examiner notes that 60/248,210 and the foreign application are not in English; thus, said applications cannot be used to support an earlier effective filing date.

Receipt is acknowledged of papers (DE 10116518.8) submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

4. The information disclosure statement filed on September 3, 2002 fails to comply with 37 C.F.R. § 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The following references were not considered for the reasons described below:

- a) Other Document AY: Incomplete citation.
- b) Other Document AZ: In complete citation.

All other documents in said Information Disclosure statement were considered as noted by the Examiner initials in the copy attached hereto.

The Examiner also notes the receipt of IDSs filed disclosing related application.

Declaration

5. The Examiner notes that the declaration filed June 12, 2002 improperly notes the filing date of 60/248,210 as November 15, 2001, not the true date of November 15, 2000. This is clearly a typographical error; no action is required by Applicants.

Compliance with the Sequence Rules

6. By virtue of the sequence listing filed on June 12, 2002 containing 12 sequences, the instant application fully complies with the sequence rules.

Objections to the Specification

7. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---Process of Fermentative Production of L-amino acids using *Enterobacteriaceae* strains with Attenuated PoxB Genes---

8. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter and for having an improper format (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the full name of the enzyme, pyruvate oxidase, for completeness. Moreover, the Abstract should be a single paragraph. Correction is required.

9. The specification is objected to for being confusing with respect to the sequence listing. The sequence listing discloses SEQ ID NOs:1-12; however, SEQ ID NO:4 is not mentioned in the specification itself. Thus, its inclusion in the sequence listing is confusing. It is unclear why said sequence is in the sequence listing if it is not described in the specification. All SEQ ID

NOs in the sequence listing must be described in the specification. Appropriate correction is required.

10. The specification is objected to for being confusing containing two descriptions of the figures; the description on pages 25-26 should be deleted. Correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “poxB gene or nucleotide sequence coding therefor” is unclear. Firstly, it is unclear how nucleotide sequences can code for a gene. Secondly, it is unclear is attenuation of *any* pyruvate oxidase (the enzyme encoded by poxB as described on page 3 of the specification) meets the limitations of the claim or if only pyruvate oxidase whose genes are named “poxB” are applicable.

12. Claims 3-4 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The metes and bounds of “genes in the biosynthesis pathway” and the “metabolic pathways that reduce the formation of the L-amino acid” are unclear. Metabolic pathways in *Enterobacteriaceae* are complex and overlapping with far-reaching effects that might produce or

reduce amino acid formation. A clear definition of which enzymes are involved is required, either from the specification or the art, for all the L-amino acids.

13. Claims 7-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The listing of the Markush members by numbers, “1, 2, 3...” is unclear since these are the same as claim numbers. The Examiner suggests using ---a, b, c...---or some similar delineation that would not be confused with claim numbers.

14. Claims 7-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The first “gene” in the Markush group is unclear since it is an operon. Must all three genes be enhanced or overexpressed? If so, must it be from the operon and not from individual genes on individual plasmids, for example? Clarification is required.

15. Claims 7-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear exactly which genes must be enhanced or attenuated in the instant claims. Take the phrase “the pyc gene coding for pyruvate carboxylase”, for example. If *E. coli* is the microorganism, must the *E. coli* pyc gene used in the methods to enhance the pyc gene or can *any* pyruvate carboxylase gene (from any organism) enhance the pyc gene in the method? Additionally, if a pyruvate carboxylase gene was named ---gene A--- (and not pyc), would its use read on the instant claims?

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16. Claims 7-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The enzyme “transhydrogenase” is unclear. On page 9 of the specification, a reference to the term in the European Journal of Biochemistry describes these genes (pntA and pntB) as encoding α and β subunits of --pyridine transhydrogenase--, which is a known enzyme. It is unclear if this is the intended enzyme in the instant claims.

Also, the words “imparting” and “coding for” are used improperly because these genes encode proteins that either impart resistance or export threonine; the genes themselves do not perform these functions. Clarification is required.

17. Claims 9-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The nature of the yjfA and ytfP genes is unclear in other than the single example provided in the specification on page 10 in *E. coli*; without a function of the encoded proteins, it is wholly unclear what similar genes in other *Enterobacteriaceae* look like. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 7-10 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 7 and 9 are drawn to methods using microorganisms with affected genes wherein the gene that is claimed solely by name and without any structural limitations; the specific genes are as follows: (1) transhydrogenase, (2) imparting homoserine resistance, (3) imparting threonine resistance, (4) coding for threonine export, (5) yjfA, and (6) ytfP.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

Unlike genes such as *poxB* encoding pyruvate oxidase and *pyc* encoding pyruvate carboxylase, the instant genes encode enzymes that do not have well known structures associated with them in the art. The instant specification describes one or two examples of each on page 9-10. In the claims, these genes are only described according to the functional characteristics (or

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name) of the enzymes they encode; no structural relationship is described or used. Thus, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure. Therefore, claims drawn to methods using microorganisms affecting in these genes are also not adequately described.

*KK
4/14/04*

19. Claims 1-~~15~~¹¹ are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for attenuating genes by their deletion, does not reasonably provide enablement for attenuating genes by substituting with attenuated alleles. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To produce the products necessary to practice the claimed methods would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or

absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

On page 3, the specification describes attenuation as including using weak promoters or alleles encoding enzymes with lower activity; and in the Examples, the *poxB* gene is deleted from *E. coli*. Deletion of any pyruvate oxidase gene in any *Enterobacteriaceae* is enabled since art-described means of identifying and deleting *poxB* genes are well known. However, sufficiently weakening unknown promoters and/or identifying alleles encoding pyruvate oxidases with lower activities would require undue experimentation. The specification provides no examples or guidance as to the construction of such attenuated *poxB* genes. The nature of the invention is such that while pyruvate oxidase is well known, alteration to reduce activity, particularly in allelic variant form, are not well known. One of skill in the art would be unable to predict the structure of such variants and, thus, would be unable to practice the claimed methods to the full extent of their scope.

The Examiner notes that this rejection applies to both attenuation of the *poxB* gene as well as attenuation of additional genes (Claims 9-10).

20. Claims 3 and 7-8 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for enhancing genes by their overexpression, does not reasonably provide enablement for enhancing genes by other means. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To

produce the products necessary to practice the claimed methods would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above.

On page 7, the specification describes enhancement as including using strong promoters or genes encoding enzymes with higher activity. Overexpression of genes to enhance them in any *Enterobacteriaceae* is enabled since art-described means of overexpressing genes are well known. However, sufficiently strengthening unknown promoters and/or identifying alleles encoding aspartate kinases, for example, with higher activities would require undue experimentation. The specification provides no examples or guidance as to the construction of such enhanced genes. The nature of the invention is such that while enzymes, such as aspartate kinase, are well known, alteration to increase activity, particularly in allelic variant form, is not well known. One of skill in the art would be unable to predict the structure of such variants and, thus, would be unable to practice the claimed methods to the full extent of their scope.

21. Claim 6 is rejected under 35 U.S.C. § 112, first paragraph, enablement, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To produce the products necessary to practice the claimed methods would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above.

No guidance or working examples of reduction of *poxB* regulatory and/or catalytic properties are described. The nature of the invention is such that the encoded enzyme catalyzes a specific reaction at a known rate; affecting such a rate requires unpredictable experimentation. The art is without examples of such enzymes. Thus, the claim is not enabled.

22. Claims 12-15 are rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To practice the instant methods, one of skill in the art is required to use MG442, TOC21R, B-12288, and/or pMAK705.

On page 12, deposit of DSM 13762 (MG442 Δ poxB); no other Δ poxB strain has specifically been deposited. The deposit information related to DSM 13762 does not enable Claims 12-13. While the instant specification contains limited deposit information, the requirements to enable such a deposit have not been fully met by the instant application. To enable the instant claims by enabling the deposit either the Δ poxB of the original strains, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the **name and full address of the depository** (37 C.F.R. § 1.801 - 1.809) (those which are in bold have not been fulfilled by the instant specification), and (5) the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative.

With respect to the TOC21R and B-12288 Δ poxB strains, these can be produced using pMAK705 and pMAK705 can be produced using publicly available materials. However, the public availability of TOC21 and B-12288 is crucial to the practice of the claimed methods. Page 21 discloses deposit of TOC21R with respect to a different patent (FA 2511032); Page 23 discloses deposit of B-12288 with respect to a different patent (US 4,391,907). While deposit is possibly guaranteed for the life of these cited patents, that is not the case for the instant patent application. Applicants are invited to perfect the deposit of the instant strains with respect to this application in particular (see above for particulars) OR risk the validity of the patent if at any time during its patent term, TOC21R and B-12288 are no longer publicly available. Since MG442 is also deposited for US 4,278,765, Applicants need not conform to the upper paragraph of this item if they are willing to risk the validity of the patent if at any time during its patent term, MG442 is no longer publicly available.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

23. Claims 1-11 are rejected under 35 U.S.C. § 102(e) as being anticipated by Rieping *et al.* (USPAP 2003/0059903) effectively filed on April 13, 2001 by means of 60/283,384.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. § 102(e). This rejection under 35 U.S.C. § 102(e) might be overcome either by a showing under 37 C.F.R. § 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 C.F.R. § 1.131.

Rieping *et al.* teach production of amino acids, particularly threonine, using *Enterobacteriaceae* with an attenuated aceA gene in addition to an attenuated poxB gene (see Claim 12 for example). All other limitations are described in other claims and are considered disclosed by way of the combination of the claims.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

24. Claims 1-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Duncan *et al.* (USPAP 2003/0119154) in view of Kramer (J. Biotechnol. (1996) 45: 1-21) and Grabau *et al.* (1984) (see IDS).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. § 102(e). This rejection under 35 U.S.C. § 103(a) might be overcome by: (1) a showing under 37

C.F.R. § 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention “by another”; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 C.F.R. § 1.131; or (3) an oath or declaration under 37 C.F.R. § 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. § 104, together with a terminal disclaimer in accordance with 37 C.F.R. § 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See M.P.E.P. § 706.02(l)(1) and § 706.02(l)(2).

Dunican *et al.* teach the production of threonine in coryneform with an attenuated *poxB* gene, as well as an attenuated *pck* gene and an enhanced *pyc* gene and *mqa* gene (see page 3). Dunican *et al.* do not teach their methods in *Enterobacteriaceae*.

Kramer teaches that *C. glutamicum* and *E. coli* are the workhorses of industrial amino acid production (see page 1).

Grabau *et al.* teach the *poxB* gene from *E. coli* (see Abstract).

At the time of the invention, it would have been obvious to one of ordinary skill in the art to practice the claimed methods by attenuating *poxB* and *pck* while enhancing *pyc* in *E. coli* to produce threonine because Dunican *et al.* specifically describe these alterations for the increase in amino acid production in coryneform bacteria and because coryneform and *E. coli* are equated

as amino acid producing bacteria by Kramer. One would have been motivated to practice the claimed invention because of the “impressive” economic impact of the industrial production of amino acids (see Kramer, page 1). One would have had a reasonable expectation of success in manipulating *E. coli* as *C. glutamicum* was manipulated by Dunican *et al.* having Grabau *et al.* in hand and using well-known molecular biology techniques of gene deletion.

Other Relevant References

25. The following are cited to complete the record:

- a) Moriya *et al.* (USPN 6,197,559) teaches overexpression (increase) of pyruvate oxidase to make glutamate as opposed to decreasing its expression, as found in the instant claims, to make different amino acids.
- b) Rieping (USPN 6,623,944) teaches attenuation of *poxB* in *E. coli* for the production of pantothenic acid; no link between pantothenic acid and amino acid production productivity is known in the art. Similarly, Dusch *et al.* (USPAP 2002/0150999) teach the same methods in Coryneform.
- c) Bastuck (USPN 6,692,946) teaches attenuation of *poxB* in *E. coli* for the production of nicotinic acid; no link between nicotinic acid and amino acid production productivity is known in the art.
- d) EP 1096013 (see IDS) was first published as CA 2322553 on April 28, 2001 and could be used as prior art against claims without priority before November 15, 2001; its disclosure is limited to the extent that Dunican *et al.* (USPAP 2003/0119154) is limited above.

Conclusion

26. Claims 1-15 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kathleen M Kerr
Examiner
Art Unit 1652